S/N 10/530790 PATENT

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Applicant:	Kosaka	Examiner:	White, Dennis Michael
Serial No.:	10/530790	Group Art Unit:	1797
Filed:	April 8, 2005	Docket No.:	10873.1670USWO
Title:	TEST PIECE FOR CREATININE MEASUREMENT		

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APPELLANT'S BRIEF ON APPEAL

Dear Sir:

This Brief is presented in support of the Notice of Appeal filed February 19, 2010, from the final rejection of Claims 1-8 and 12-16 of the above-identified application, as set forth in the Office Action mailed August 19, 2009 and maintained in the Advisory Action mailed February 18, 2010.

Please charge our Deposit Account No. 50-3478 in the amount of $540.00 to cover the required fee for filing this Brief.

I. REAL PARTY IN INTEREST

The application pending for this appeal has been assigned to ARKRAY, Inc., of Kyoto, Japan.

II. RELATED APPEALS AND INTERFERENCES

The Assignee, the Assignee's legal representatives, and the Appellant are unaware of any other appeals or interferences that will affect, be directly affected by or have a bearing on the Board's decision in this Appeal.

III. STATUS OF CLAIMS

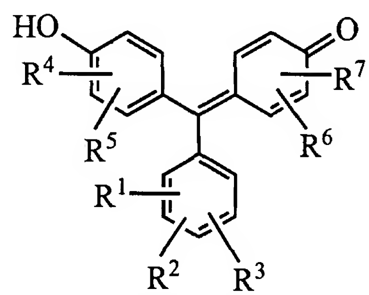
Claims 9-11 and 17-18 are canceled. Claims 1-8 and 12-16 are pending. Claims 1-8 and 12-16 are the subject of this Appeal. Appendix A attached herewith provides a copy of the claims in this Appeal.

IV. STATUS OF AMENDMENTS

A Response to the final Office Action was filed on January 19, 2010, under 37 C.F.R. § 1.116. By way of Advisory Action mailed February 18, 2010, the Response was considered, but deemed as not placing the application in condition for allowance.

V. SUMMARY OF CLAIMED SUBJECT MATTER

Independent claim 1, the sole dependent claim in this application, is directed to a test piece for creatinine measurement (see page 2, lines 17-18 of the specification). The test piece of claim 1 comprises a compound expressed by the following formula (1)



where R^1 represents H, SO_3X or COOX, R^4 and R^6 represent OH, SO_3X, or COOX and are either the same or different, R^2, R^3, R^5 and R^7 represent H, OH, Cl, Br, I, NO_2, NO, or CH_3 and are either the same or different, and Xs in the R^1, R^4 and R^6 represent H, Na, K, or NH_4 and are either the same or different (see page 2, lines 19-27 of the specification).

The test piece of claim 1 further comprises a transition metal or its salt that forms a colored complex with the compound, the transition metal being Pd(II) (page 6, lines 30 and 33 of the specification).

The test piece recited in claim 1 can be used to evaluate the presence or absence of creatinine and to determine the amount of creatinine in a sample (see page 2, line 28 to page 3, line 19 of the specification). The measurement of creatinine using the test piece of claim 1 is

based upon the degree of inhibition by creatinine of the formation of a colored complex that is formed between the compound represented by the formula (I) and Pd(II) (see page 3, lines 7-12 of the specification). Advantageously, the test piece recited in claim 1, unlike conventional creatinine measurement systems, allows creatinine to be measured without the use of strong alkaline reagents, expensive enzymes or a special facility for microdeterminations (see page 1, line 36 to page 2, line 8 and page 2, line 28 to page 3, line 19 of the specification). Moreover, the test piece recited in claim 1 allows creatinine to be measured at room temperature (page 3, lines 12-13 of the specification). Thus, unlike conventional creatinine measurement systems that involve the use of enzymes, it is not necessary to adjust the reaction temperature to an optimum temperature of the enzyme when using the test piece of claim 1 (page 3, lines 13-15 of the specification). As such, the reaction time can be reduced as compared to creatinine measurement systems that involve the use of enzymes when using the test piece of claim 1 to measure creatinine (see page 3, lines 12-17 of the specification). Accordingly, the test piece of claim 1 allows creatinine measurements to be performed quickly and easily *(Id.)*.

VI. GROUNDS OF REJECTION TO BE REVIEWED ON APPEAL

The following issues are raised in the final rejection:

1. Whether claims 1-8 and 12-16 are obvious over Mori et al. (Chem. Pharm. Bull.,1983) in view of Kosaka (US 2002/0037591).

VII. ARGUMENT

A. Claims 1-8 and 12-16 are patentable over Mori et al. (Chem. Pharm. Bull., 1983) in view of Kosaka (US 2002/0037591)

Claims 1-8 and 12-16 were rejected under 35 USC 103(a) as being unpatentable over Mori et al. (Chem. Pharm. Bull., 1983) in view of Kosaka (US 2002/003759 1). Applicant submits that when Mori and Kosaka are each understood as a whole, the combination of the references would not have yielded a predictable result of a test piece for measuring creatinine, as required by claim 1.

Mori is directed to a system for measuring creatinine. Creatinine is a <u>non-protein</u> and is generally found in human urine (see page 1390, lines 46-47 of Mori). Mori's investigation is

based on the finding that the presence of creatinine decreases the absorbance of the *o*-hydroxyhydroquinonephthalein (Qn.Ph.)-Pd(II) complex (herein after, "QnPh-Pd(II) complex"; see page 1389, lines 9-13 of Mori), and aims to develop suitable conditions for a creatinine detection system involving the use of the QnPh-Pd(II) complex (see page 1389, lines 14-15 of Mori). Mori indicates that suitable conditions for their reaction system are as follows: (1) a pH of 5.3 to 5.7, (2) a reaction temperature at 60°C and (3) a reaction time of 45-60 minutes (see page 1390, lines 5-11 and 24-29 of Mori). Mori then confirms the effects of creatinine on the absorption spectra of the QnPh-Pd(II) complex under the suitable conditions (pH of 5.5, temperature of 60°C and reaction time of 45-60 minutes; see Standard Procedure under the Experimental section on page 1389 and Figure 1 on page 1390 of Mori).

As shown in Fig. 1, sample A, which contains only QnPh, does not exhibit an absorption peak at 615 nm, whereas sample B, which contains QnPh-Pd(II), exhibits an absorption peak at 615 nm. This data indicates that QnPh-Pd(II) forms a complex. As shown in sample C, which contains QnPh-Pd(II) and creatinine, the absorption peak at 615 nm is lowered, and as shown in samples D and E, which contain QnPh-Pd(II) and higher amounts of the creainine as compared to sample C, the absorption peak at 615 nm is lowered even further. This data indicates that creatinine inhibits QnPh-Pd(II) complex formation by a competitive binding mechanism under conditions of pH 5.5, a temperature of 60 °C and reaction time of 45 minutes.

Mori then further investigates the effects of protein on creatinine inhibition of the QnPh-Pd(II) complex formation (see page 1390, lines 35-43 and Table 1 on page 1391). Mori indicates that protein does not affect the sensitivity for measuring creatinine (see page 1391, lines 1-2; see also see page 1389, line 5, where Mori indicates that examples of Jaffe chromogens include protein), thereby suggesting that protein has no effect on creatinine inhibition of the QnPh-Pd(II) complex formation under conditions of pH 5.5, a temperature of 60 °C and reaction time of 45 minutes.

The test piece of claim 1 comprises the compound represented by the formula (1) and Pd(II) or its salt, where the compound and Pd(II) or its salt forms a colored complex. Mori does not disclose that their creatinine measurement system includes a compound represented by the formula (1). Furthermore, Mori does not provide any guidance or experimental data to suggest that QnPh can be substituted with any other compound and achieve a system for creatinine

measurement. That is, their investigation is based on the past finding that creatinine inhibits the formation of the QnPh-Pd(II). Their investigation is directed to finding suitable conditions where interfering substances such as protein do not affect the measurement of creatinine. Mori's objective is to configure their system so that their system can be utilized with samples such as urine where protein is present. Thus, when Mori is understood as a whole, it is clear that the reaction conditions in Mori's system is adjusted specifically for the complex formation reaction between QnPh and Pd(II) in the presence of creatinine, and the reference fails to provide any basis to show that there would have been a reasonable expectation success in substituting QnPh with another compound and achieve a system for measuring creatinine.

Kosaka is directed to a system for measuring protein (paragraph [0014] of Kosaka). Kosaka aims to develop a protein measurement system with sufficient sensitivity to measure minute amounts of protein in urine (paragraph [0022] of Kosaka). Kosaka teaches that their system is based on a phenomenon where QnPh or pyrocatechol violet binds specifically to indium to form a complex, the thus formed complex binds to protein to shift the wavelength (see paragraph [0025] of Kosaka). As such, it is clear from this discussion that Kosaka teaches that protein does not inhibit the complex formation reaction between QnPh or pyrocatechol violet and indium, but rather, directly binds to the QnPh or pyrocatechol violet and indium complex once the complex is formed. Kosaka teaches the following reactions conditions: (1) a pH of 2.7, (2) a reaction temperature at 37°C and (3) a reaction time of 10 minutes (paragraph [0038] of Kosaka). Kosaka develops a calibration curve of their protein measurement system using standard protein solutions (paragraph [0039] and Figure 1), and then measures 60 urine samples using their protein measurement system and compares their results with results obtained using known protein measurement systems (paragraph [0040]). Kosaka confirms that their protein measurement system correlates well with known protein measurement systems (paragraph [0040]), thereby indicating that substances commonly present in the urine, such as creatinine, do not affect the sensitivity of Kosaka' s protein measurement system.

Thus, give that in Kosaka' s protein measurement system, the amount of binding between protein and the QnPh- indium complex and the amount of protein are directly proportional to one another, and further given that this relation is not affected by the presence of creatinine, it is clear that in Kosaka' s protein measurement system, QnPh is not involved in a competitive binding

mechanism under the reaction conditions of (1) a pH of 2.7, (2) a reaction temperature at 37°C and (3) a reaction time of 10 minutes.

On the other hand, as discussed above, in Mori's system, QnPh is involved in a competitive binding mechanism where a non-protein, namely creatinine, inhibits the complex formation reaction between QnPh and Pd(II), as opposed to protein binding directly to the complex formed by the complex formation reaction between QnPh and indium, under conditions of (1) a pH of 5.3 to 5.7, (2) a reaction temperature at 60°C and (3) a reaction time of 45 minutes, as opposed to conditions of (1) a pH of 2.7, (2) a reaction temperature at 37°C and (3) a reaction time of 10 minutes.

Thus, it is clear that QnPh is functioning in a completely different manner in Mori and Kosaka's system. That is, in Mori's creatinine measurement system, QnPh binds to Pd(II) in the presence of protein, and competes for binding to Pd(II) with creatinine under conditions of (1) a pH of 5.3 to 5.7, (2) a reaction temperature at 60°C and (3) a reaction time of 45 minutes. In Kosaka's system, QnPh binds to indium to form a complex without competing with creatinine for binding to indium under conditions of (1) a pH of 2.7, (2) a reaction temperature at 37°C and (3) a reaction time of 10 minutes, and once the complex between QnPh and indium is formed, protein binds to the complex.

Kosaka indicates that in their protein measurement system, QnPh is interchangeable with pyrocatechol violet (see paragraph [0025]). However, Kosaka fails to provide any guidance or experimental data to suggest that pyrocatechol violet can form a complex with Pd(II), let alone teach or suggest that pyrocatechol violet can compete with creatinine for binding to Pd(II) under conditions of(1) a pH of 5.3 to 5.7, (2) a reaction temperature at 60°C and (3) a reaction time of 45 minutes so that pyrocatechol violet could be used in a creatinine measurement system as taught by Mori. As indicated above, when Mori is understood as a whole, it is clear that the reaction conditions in Mori's system is adjusted specifically for the complex formation reaction between QnPh and Pd(II) in the presence of creatinine. Thus, when Mori and Kosaka are each understood as a whole, it is clear that QnPh is not functioning in such a way that the application of the interchange of QnPh with pyrocatechol violet in Kosaka's protein measurement system to Mori's creatinine measurement system would yield a predictable solution, and therefore, the combination of the references would not have yielded a predictable result of a test piece for

measuring creatinine, as required by claim 1.

Accordingly, for at least the above reasons, claim 1 is patentable over Mori and Kosaka, taken alone or together. Claims 2-8 and 12-16 are also patentable over the references since they depend from claim 1 that is allowable. Reversal of the rejection is respectfully requested.

VIII. CONCLUSION

Appellant submits that the rejections of claims 1-8 and 12-16 are untenable for the reasons set forth above and should be reversed.

Please charge any additional fees or credit any overpayment to Hamre, Schumann, Mueller & Larson Deposit Account No. 50-3478.

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PATENT TRADEMARK OFFICE

Respectfully submitted,

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Date: March 23, 2010

By ______________________
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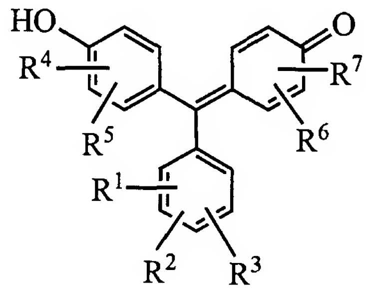
APPENDIX A - PENDING CLAIMS

1. (rejected) A test piece for creatinine measurement comprising:

a compound expressed by the following formula (1)



(1)

where R^1 represents H, SO_3X or COOX,

R^4 and R^6 represent OH, SO_3X, or COOX and are either the same or different,

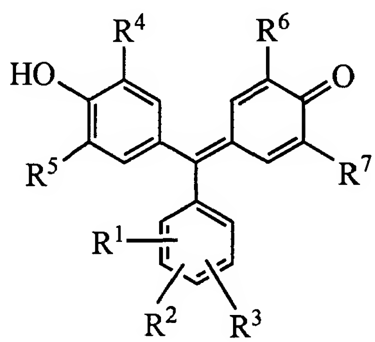
R^2, R^3, R^5 and R^7 represent H, OH, Cl, Br, I, NO_2, NO, or CH_3 and are either the same or different, and

Xs in the R^1, R^4 and R^6 represent H, Na, K, or NH_4 and are either the same or different, and

a transition metal or its salt that forms a colored complex with the compound,

wherein the transition metal is Pd(II).

2. (rejected) The test piece for creatinine measurement according to claim 1, wherein the compound is expressed by the following formula (2)



(2)

where R^1 represents H, SO_3X, or COOX,

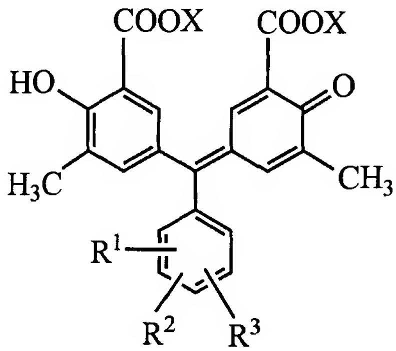
R^4 and R^6 represent OH, SO_3X, or COOX and are either the same or different,

R^2, R^3, R^5 and R^7 represent H, OH, Cl, Br, I, NO_2, NO, or CH_3 and are either the same or

different, and

Xs in the R^1, R^4 and R^6 represent H, Na, K, or NH_4 and are either the same or different.

3. (rejected) The test piece for creatinine measurement according to claim 2, wherein the compound is expressed by the following formula (3)



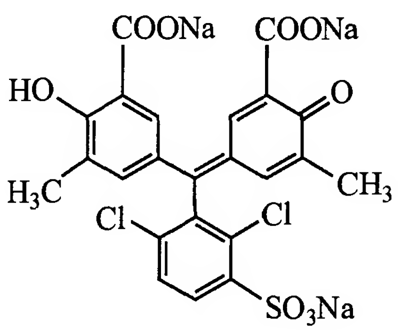
(3)

where R^1 represents H, SO_3X, or COOX,

R^2 and R^3 represent H, OH, Cl, Br, I, NO_2, NO, or CH_3 and are either the same or different, and

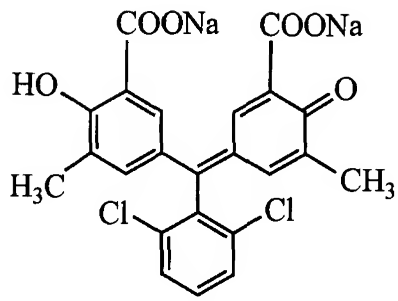
Xs represent H, Na, K, or NH_4 and are either the same or different.

4. (rejected) The test piece for creatinine measurement according to claim 1, wherein the compound is expressed by the following formula (4)



(4)

5. (Original) The test piece for creatinine measurement according to claim 1, wherein the compound is expressed by the following formula (5)



(5)

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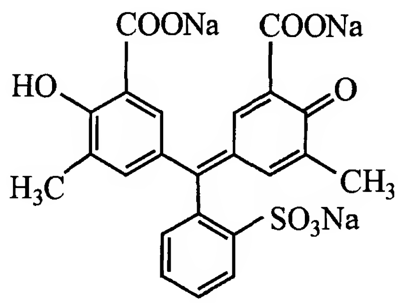
6. (rejected) The test piece for creatinine measurement according to claim 1, wherein the compound is expressed by the following formula (6)



(6)

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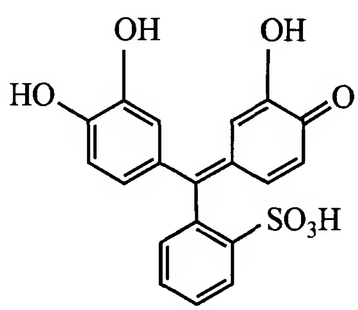
7. (rejected) The test piece for creatinine measurement according to claim 1, wherein the compound is expressed by the following formula (7)



(7)

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8. (rejected) The test piece for creatinine measurement according to claim 1, wherein the compound is included in a porous material.

9-11. (Canceled)

12. (rejected) The test piece for creatinine measurement according to claim 1, wherein the compound (A) and the metal or its salt (B) are present at a ratio (molar ratio A:B) of 30:1 to 1:15.

13. (rejected) The test piece for creatinine measurement according to claim 1, further comprising a buffer agent.

14. (rejected) The test piece for creatinine measurement according to claim 13, wherein the compound (A) and the buffer agent (C) are present at a ratio (molar ratio A:C) of 1:10 to 1:1000.

15. (rejected) The test piece for creatinine measurement according to claim 1, further comprising a surfactant.

16. (rejected) The test piece for creatinine measurement according to claim 15, wherein the compound (A) and the surfactant (D) are present at a ratio (molar ratio A:D) of 50:1 to 3:1.

17-18. (Canceled)

APPENDIX B - EVIDENCE

Not applicable

APPENDIX C - RELATED PROCEEDINGS

Not applicable